IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

LIFE TECHNOLOGIES CORPORATION, and APPLIED BIOSYSTEMS, LLC,	§	
Plaintiffs,	§	CIVIL ACTION NO. 2:09-cv-00283
v.	§	
BIOSEARCH TECHNOLOGIES, INC., BIO-SYNTHESIS, INC., and EUROFINS MWG OPERON INC.,	§	
Defendants.	§	

PLAINTIFFS LIFE TECHNOLOGIES CORPORATION AND APPLIED BIOSYSTEMS, LLC'S OPPOSITION TO THE MOTION TO RECONSIDER THE SEPTEMBER 22, 2011 CLAIM CONSTRUCTION ORDER

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I. INTRODUCTION

The Court issued a detailed twelve-page claim construction order in which Magistrate Judge Everingham correctly construed the eight terms disputed by the parties. Mem. Op. and Order, Dkt. No. 212 ("Order"). The Order only issued after the Court's consideration of 70 pages of briefing, 32 exhibits, and arguments offered at a two-hour claim construction hearing. During that hearing, Defendants Biosearch Technologies, Inc. and Eurofins MWG Operon Inc. ("Defendants") used only 31 of their allotted 90 minutes. *See* Dkt. No. 207. When Defendants ended their presentation, Magistrate Judge Everingham specifically advised them that "I don't allow sur-rebuttal, so take your shots now. Don't be holding back." Ex. 1,[1] Aug. 23, 2011 Claim Construction Hearing Tr., at 54:21-23. Defendants acknowledged that they understood, but offered nothing further. *Id.* at 54:24. One month later, the Court rejected Defendants' position on each of the eight terms at issue, providing detailed reasons for its ruling.

After losing on every disputed term, Defendants now have more to say. Defendants ask the Court to revisit three of the eight terms. Plaintiffs Life Technologies Corporation and Applied Biosystems, LLC ("Plaintiffs") submit that Judge Everingham's constructions are correct and therefore oppose Defendants' motion. Each of Defendants' arguments is substantively flawed and should be rejected.

II. "QUENCHER MOLECULE"

The Magistrate's construction of the term "quencher molecule" is taken nearly verbatim from the specifications of four of the five patents. The Court rejected Defendants' construction that ignored the express definition of the term as set forth in the specification by the patentees. Order at 10-11. Defendants now move for reconsideration of the Court's ruling because they

[1] Unless otherwise noted, exhibit numbers refer to exhibits filed with this opposition.

allege that "[r]ather than consider all the intrinsic evidence, the Court essentially focused solely on the specification." Defs.' Mot. to Recons., Dkt. No. 218 ("Motion" or "Motion for Reconsideration"), at 1.

A. The Court Properly Construed "Quencher Molecule" in Accord With the Express Definition in the Specification.

The *en banc* Federal Circuit has directed that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005). As the Court recognized, this is exactly what the patentees did. *See* Dkt. No. 181-1 at col. 1, ll 36-41 ("A quencher molecule is a molecule capable of absorbing the fluorescence energy of an excited reporter molecule, thereby quenching the fluorescence signal that would otherwise be released from the excited reporter molecule.").[2] Defendants do not deny this fact, but still improperly rely on the standard for determining a term's ordinary meaning. Motion at 2 ("[W]e cannot look at the ***ordinary meaning*** of the term . . . in a vacuum. Rather, we must look at the ***ordinary meaning*** in the context of the written description and the prosecution history.").[3] It is not the ordinary meaning of the term that is at issue. The patentees expressly defined "quencher molecule" and that definition governs, even if it differs from the ordinary meaning. *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002) ("[T]he claim term will not receive its ordinary meaning if the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in either the

[2] The asserted patents are U.S. Pat. Nos. 5,538,848; 5,723,591; 5,876,930; 6,030,787; and 6,258,569. Individually, each is referred to by its final three numbers; collectively they are referred to as "the Livak Patents." The specifications of the '591, '930, '787, and '569 Patents are essentially identical and all claim priority to the '848 Patent. Therefore, the citations used herein that reference the '848 Patent are applicable to all of the Livak Patents, while references to the '591 apply to it as well as to the specification of the '930, '787, and '569 Patents.

[3] Unless otherwise noted, all emphasis in quotations is added.

specification or prosecution history.").

Moreover, the written description, the claim language, and the prosecution history all support and confirm the correctness of the Court's construction as the express definition. For example, the written description not only expressly defines the term with the Court's construction, it also directly contradicts Defendants' construction. *See* Order at 10; *see also* Dkt. No. 181 at col. 5, ll. 46-48 ("[Q]uencher molecules . . . may or may not be fluorescent.").

Similarly, the patents' claims show that the patentees "knew how to define the scope of the quencher molecule when [they] chose to do so" – some claims are directed to "a quencher molecule," while others are directed to "a fluorescent quencher molecule." Order at 10. Just as the Federal Circuit held that the claim term "'steel baffles' . . . strongly implies that the term 'baffles' does not inherently mean objects made of steel," the use of the term "fluorescent quencher" strongly implies that the term "quencher" does not inherently mean an element that is fluorescent. *Phillips*, 415 F.3d at 1314.

And as the Court correctly noted, the prosecution history shows "no intention on the part of the patentee to disavow quenchers that do not emit light." Order at 11. Indeed, the prosecution history specifically recognizes that not all quenchers are fluorescent. Patentees commented on an amendment by stating that "the Examiner objects that the quencher is not specified as being fluorescent. In response, Applicants amend claim 17 to specify a fluorescent quencher." Dkt. No. 181-11 at 11. If all quenchers were fluorescent, the amendment would have been unnecessary. Indeed, all of the intrinsic evidence supports the Court's construction.

B. The Court Construed "Quencher" Consistently Throughout the Patents.

Defendants assert that the Court improperly construed "quencher molecule" differently for different claims in the Livak Patents. This challenge fails on two levels. First, Defendants' own authority recognizes that claim terms may be given different meanings where "it is clear

from the specification and prosecution history that the terms have different meanings at different portions of the claims." *Schoenhaus v. Genesco, Inc.*, 440 F.3d 1354, 1357 (Fed. Cir. 2006) (emphasis omitted); *see also Phillips* at 1314 ("[C]laim terms are ***normally*** used consistently throughout the patent."). Thus, Defendants' premise that "The Same Term Cannot Be Construed Differently for Different Claims" (Motion at 2) reflects a misunderstanding of applicable law.

Second, this challenge also fails because the Court in fact did not construe "quencher molecule" differently for different claims. The Court gave one construction of "quencher molecule." *See* Order at 10-11. Defendants inaccurately assert that "[t]he Court has agreed that some of the claims require ***the term*** 'quencher' be interpreted as a 'fluorescent quencher.'" Motion at 3 (emphasis omitted). But the Court did not hold that the ***term*** "quencher" sometimes meant "fluorescent quencher." Rather, the court held that "the ***claims*** of the Livak patent require, in some instances, that the quencher molecule emit light so that a certain ratio might be determined." Order at 11. The claims require this, not through a construction of the word "quencher," but rather through a different claim limitation. Specifically, claim 24 of the '848 Patent includes a limitation reciting "the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule." Dkt. No. 181 at col. 16, ll. 22-23. By referring to a fluorescence intensity of the quencher molecule in the denominator, this particular claim limitation requires the presence of a quencher molecule whose fluorescence intensity is not zero. *See* Ex. 1 at 9:23-10:12. But as this limitation already includes the requirement that the quencher be "fluorescent," nothing in this limitation narrows the meaning of the word "quencher" itself.

C. The Court's Construction Does not Render "Nonsensical Results," and Courts Cannot Rewrite Even "Nonsensical" Claims.

Defendants argue that the Court's construction of quencher would result in a nonsensical result for one claim – claim 24 of the '848 Patent. As discussed above, the term "the ratio of the

fluorescence intensities of said reporter molecule to said quencher molecule" adds an additional limitation regarding fluorescence, independent of the word "quencher." The Court's construction of "quencher" thus does not render the claim nonsensical. The Court properly rejected that this claim would be "nonsensical" under the Court's construction.

Moreover, if this one claim were found to be nonsensical (which it is not), courts will not rewrite claims that are otherwise unambiguous. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1366 (Fed. Cir. 2011) (citing *Chef Am., Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1374 (Fed. Cir. 2004)). Instead, courts will only construe claims to preserve their validity where they are "amendable to more than one construction." Dkt. No. 192 at 6; *see also Phillips*, 415 F.3d at 1327-28 ("[T]he claim term at issue is not ambiguous. Thus, . . . [t]he doctrine of construing claims to preserve their validity, a doctrine of limited utility in any event, therefore has no applicability here."). Likewise, as Defendants' own authority recognizes, courts only "strive, ***where possible***, to avoid nonsensical results in construing claim language." *AIA Eng'g Ltd. v. Magotteaux Int'l S/A*, No. 2011-1058, 2011 U.S. App. LEXIS 18125, at *28 (Fed. Cir. Aug. 31, 2011) (citation omitted). Thus, Defendants' premise that "a claim term cannot be construed to render 'nonsensical' results" is, at best, an over-simplification of a claim construction canon.

Indeed, Defendants fail to cite any case where a court rejected an unambiguous construction to avoid a "nonsensical result," or to otherwise preserve validity. *See Schoenhaus*, 440 F.3d at 1356-57 (using nonsensical results only after concluding the rejected construction derived from descriptions of the "invention" rather than of the claim term at issue); *Becton, Dickinson & Co. v. Tyco Healthcare Grp., LP*, 616 F.3d 1249, 1255 (Fed. Cir. 2010) (using a nonsensical result to confirm a construction for which "the specification comports with the plain language of the claims, fully supporting" the adopted construction); *Bd. of Regents of the Univ.*

of Tex. Sys. v. BenQ Am. Corp., 533 F.3d 1362, 1370 (Fed. Cir. 2008) (using a nonsensical result to reject a construction without clear support in specification which also "d[id] not square with the prosecution history."); *AIA Eng'g*, 2011 U.S. App. LEXIS 18125 at *26-27 (considering a contradictory result of the plain and ordinary meaning only after concluding that "the intrinsic evidence reveals that the patentee acted as his own lexicographer.").

In sum, to rewrite the express definition of this term to add another limitation would be to rewrite the claims of the patent, which the Federal Circuit forbids. Defendants misstate and misapply the law of claim construction in a belated attempt to divert attention from the correct construction of the term "quencher molecule."

D. The Patentees did not Disavow Non-Fluorescent Quenchers.

Defendants point to patentees' amendment from "quencher molecule" to "fluorescent quencher molecule" in one claim[4] as a purported "disavowal" of the scope of "quencher." Far from disavowing non-fluorescent quenchers, this demonstrates that not all quenchers are fluorescent by adding the limiting adjective "fluorescent" to "quencher." Motion at 5; *see also Phillips*, 415 F.3d at 1314 ("'[S]teel baffles,' . . . strongly implies that term 'baffles' does not inherently mean objects made of steel.").

The Court properly construed "quencher molecule" based on the patentees' express definition, consistent with the entire intrinsic record. Defendants' motion for reconsideration should be denied.

III. "A HAIRPIN STRUCTURE"

The Court adopted a construction of "a hairpin structure" that is essentially the express definition of the term recited in four out of the five asserted Livak patents. Order at 11. The

[4] After this amendment, patentees used "fluorescent quencher molecule" in several other claims which contained the same ratio.

patentees here acted as their own lexicographer, and the Court adopted a construction premised upon the express definition of the term.

Ignoring the express definition of the term, Defendants ask this Court to adopt a construction divorced from that manifestation of the inventors' intended meaning for the term. Defendants rely primarily on extrinsic evidence, which cannot trump a patentee's clear expression of a term's scope within the patent's specification.

A. The Court Properly Adopted Patentees' Definition of "a Hairpin Structure."

The express definition of "a hairpin structure" within the Livak patents narrows the basic meaning of the word "hairpin" as used in the general field of molecular biology. A hairpin is generally understood to be a structure in which a strand of DNA hybridizes with itself to form a stem where the two parts of the strand have hybridized and a loop of single stranded DNA connecting the two parts of the stem. *See generally* Dkt. No. 180 at 2-5. This structure can occur, for example, when a stretch of bases in one part of a DNA strand happen to be complementary to a stretch of bases in another part of the same strand – those complementary portions forming the "stem" and the portion of the strand between them can forming the "loop" structure.

1. The Written Description Supports the Patentees' Definition.

While the plain and ordinary meaning of "hairpin structure" does not require reporter and quencher molecules, the patentees used "hairpin structure" to mean something distinct, as they are permitted to do. *See Phillips*, 415 F.3d at 1316; *CCS Fitness*, 288 F.3d at 1366.[5] In particular, the Livak patent specification discusses hairpin structures and distinguishes the Livak probes from prior art probes that were designed to form a hairpin that brought a reporter and a

[5] Patentees' definition is hardly unique – indeed, Defendant Biosearch's own patents use the identical definition of hairpin structure. *See* Dkt. No. 180 at 17.

quencher on opposite ends of a probe together:

> Probes containing a reporter molecule – quencher molecule pair have been developed for hybridization assays where the probe forms ***a hairpin structure, i.e., where the probe hybridizes to itself to form a loop such that the quencher molecule is brought into proximity with the reporter molecule in the absence of a complementary nucleic acid sequence to prevent the formation of the hairpin structure.*** WO 90/03446; European Patent Application No. 0 601 889 A2. When a complementary target sequence is present, hybridization of the probe to the complementary target sequence ***disrupts the hairpin structure and causes the probe to adopt a conformation where the quencher molecule is no longer close enough to the reporter molecule*** to quench the reporter molecule. As a result, the probes provide an increased fluorescent signal when hybridized to a target sequence then when unhybridzed. ***Probes including a hairpin structure have the disadvantage that they can be difficult to design*** and may interfere with the hybridization of the probe to the target sequence.

Dkt. No. 181-1 at col. 1, ll. 46-63.[6] The first emphasized section in the quote above explicitly defines that "a hairpin structure" includes a relationship between a reporter and a quencher using the abbreviation "*i.e.*" *Id.* at col. 1, ll. 48-53. The second emphasized section reiterates this definition. *Id.* at col. 1, ll. 56-59. The final emphasized section shows "hairpin structures" in the Livak Patents are intentionally "design[ed]" with a degree of precision that can be "difficult." *Id.* at col. 1, ll. 60-62. But a structure resulting from binding of nucleotides anywhere on a strand of DNA is not difficult to design, and indeed frequently happens unintentionally.[7] Indeed, adopting Defendants' construction would read a preferred embodiment out of the claims and so is disfavored. *See* Dkt. No. 180 at 16; Dkt. No. 201, at 4 n.9; Ex. 1 at 14:25-16:8.

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[6] Defendants themselves recognize that in this definition "reporters and quenchers . . . are brought into proximity when the hairpin structure is present." Motion at 6. It follows that one of the features of the hairpin is this very bringing reporters and quenchers into proximity with each other.

[7] Indeed, this is why Defendants are seeking this construction. Since "a hairpin structure" is a negative limitation added to exclude prior art structures, Defendants are seeking ignore the actual definition to later excuse some of their infringing probes which may happen to contain some random base pair complementarity.

2. The References Cited in the Specification Support the Court's Construction.

Rather than contradict the Court's claim construction as Defendants allege, the two references cited in the above definition support it. The first reference discloses the use of probes that contain "[s]witch sequences [that] are complementary and hybridize to each other . . . forming the stem . . . of a 'hairpin' secondary structure," to use the "change in the switch sequences in the above probe molecules to generate a detectable signal." Dkt. No. 192-2 at 11:5-10, 13:3-6. This language describes using a hairpin structure to create a signal based on whether the probe forms a hairpin. In other words, this hairpin structure is designed to bring together a reporter and quencher on a probe. *See generally* Dkt. No. 180 at 3-5. Defendants claim that this reference "contains fourteen figures including hairpin structures, none of which includes a single reporter or quencher molecule." Motion at 6 (emphasis omitted). This is circular logic. Defendants have looked for pictures of what they believe should be called "hairpins," and then reject the patentees' express definition because it does not match Defendants' pictures. Further, Defendants look at the figures in isolation, ignoring the fact that this reference discusses use of hairpins as "switches" for turning reporting signals on and off.

Similarly, the second reference cited discloses probes where "only when one or more imperfect hairpins are formed, one of the donor label moieties and one of the acceptor label moieties are in close proximity to allow resonance energy transfer between them." Dkt. No. 181-8, at 2:33-35. As a reporter is a donor and a quencher is an acceptor, the Court's construction closely matches the prior art referenced.

The written description and the references patentees cite in the written description display a consistent and clear definition of "hairpin structure." The Court adopted that definition. The Court should reject Defendants' challenge to this construction and affirm its earlier ruling.

B. Far From Disclaiming the Express Definition of "Hairpin Structure," the Prosecution History Confirms it.

Plaintiffs previously showed that the patentees' express definition of "a hairpin structure" is confirmed by the prosecution history. *See* Dkt. No. 180 at 13-16. Now, for the first time, Defendants allege that the patentees disclaimed the scope of this definition during prosecution by stating that the express "definition for the term 'hairpin structure' ***is consistent with*** other art references" that discuss the ordinary meaning of the term hairpin. Motion at 7 (citation omitted).[8] Not only does this statement not rise to the level of a clear disclaimer of claim scope, but it supports the Court's construction. *See Inverness Med. Switzerland GmbH v. Warner Lambert Co.*, 309 F.3d 1373, 1382 (Fed. Cir. 2002) ("[W]e are . . . not convinced that the prosecution history demonstrates that the patentee clearly was using the disputed language in a limited sense that would foreclose the broader dictionary definitions . . . . It is inappropriate to limit a broad definition of a claim term based on prosecution history that is itself ambiguous."). The defined 'hairpin structure' has all the features of the plain and ordinary meaning of the term, as well as an additional feature (bringing the reporter and quencher into proximity) used in the dual-labeled probe prior art.

In sum, the Court properly construed "a hairpin structure" based on the patentees' express definition and consistent with the entire intrinsic record. The Court's construction should be affirmed and Defendants' Motion for Reconsideration should be denied.

IV. "MONITORING THE FLUORESCENCE"

The Order correctly holds that "the term 'monitoring the fluorescence' needs no further construction." Order at 18. Defendants argued that "monitoring the fluorescence" should be

[8] By waiting to raise this argument for the first time in their Motion, Defendants have waived this argument.

limited to "only at the conclusion of an amplification reaction." *See* Dkt. No. 201 at 6-7. They argued for this limitation because they asserted that was "the state of the art that existed a[t] the time of this patent was filed for." Ex. 1 at 35:22-36:3. The Court rejected this argument, holding that "[t]he Livak patents . . . cite to 1992 and 1993 publications disclosing monitoring fluorescence during reactions in 'real time.'" Order at 17.

The Livak Patents discuss "real time measurements of amplification products during a PCR." Dkt. No. 181 at col. 1, ll. 54-55. A "PCR reaction" is a cyclical amplification of DNA. During a cycle, each copy of the particular target sequence of DNA is duplicated (or "amplified"), generally doubling the number of target DNA molecules. Thus, if a PCR reaction began with two copies of a particular target DNA sequence, in general, four copies of the DNA sequence would exist at the end of the first cycle, eight copies at the end of the second cycle, sixteen at the end of the third cycle, and so on.[9] This doubling would continue until the reaction used up one or more of the materials needed to copy the DNA and could not continue or until the reaction reached its set number of cycles. At the conclusion of a PCR reaction the number of DNA molecules of the target sequence has been dramatically amplified.

Defendants argue that one of skill in the art in 1994 would understand that "monitoring" such an amplification reaction would take place "only at the conclusion of [the] amplification reaction," thereby only measuring the final number of copies made. As discussed below, however, the intrinsic and extrinsic evidence show that one of ordinary skill in the art would have understood "monitoring" to mean observing or determining the generation of product at intermediate cycles as the reaction progressed.

[9] In theory the number of template molecules can double in each round, but in practice one does not always achieve perfect doubling in each round.

A. The Court Properly Concluded That a Skilled Artisan Would Have Understood "Monitoring The Fluorescence" to Have its Ordinary Meaning.

Courts interpret claims based on "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips*, 415 F.3d at 1313. Defendants incorrectly argue that giving the term "monitoring the fluorescence" its ordinary meaning would "improperly . . . capture later-developed technology." Motion at 11. But the only two cases relied on by Defendants involved interpretation of particular words having a temporal dimension in context (*e.g.*, the words "normally" and "conventional") that the Court concluded were "governed by their ordinary and customary meanings, and that, ***in view of their implicit time-dependence***, the district court did not err in construing the literal scope of the claim limitations qualified by those terms as being limited to technologies existing at the time of the invention." *PC Connector Solutions LLC v. SmartDisk Corp.*, 406 F.3d 1359, 1363 (Fed. Cir. 2005); *see also Kopykake Enters., Inc. v. Lucks Co.*, 264 F.3d 1377, 1382-83 (Fed. Cir. 2001). No such temporal dimension or "implicit time-dependence" exists here. As a result, the only issue for claim construction is how one of skill in the art would have understood "monitoring" at the time of the invention.

The intrinsic record shows that one of skill in the art would have understood "monitoring the fluorescence," to have its ordinary meaning, that is, to refer to monitoring fluorescence ***during*** reactions. For example, the Livak specifications state that "real time ***monitoring*** of an amplification reaction permits . . . taking into account ***the history*** of the relative construction values ***during the reaction***." Dkt. No. 181 at col. 1: ll 44-49. As the Court noted, the Livak Patents cite to 1992 and 1993 publications by Higuchi et al. disclosing monitoring fluorescence ***during*** reactions in "real time." *Id.* at col. 1, ll. 37-38. For example, the 1992 article teaches "continuous ***monitoring***" of fluorescence during reactions of "a PCR ***undergoing***

thermocycling." Dkt. No. 201-1 at 415. The 1993 article discloses "[c]ontinuous ***monitoring***" to "capture ***fluorescence*** images of an array of PCRs." Dkt. No. 201-2 at 1026. With this disclosure, one of skill in the art would have understood "monitoring" to mean during a reaction.

Defendants raise two attorney argument challenges: that Defendants were unable to find other art between 1992 and 1996 that used real time monitoring and that the methods used in one of the Higuchi papers were not simple. Both of these arguments fail as detailed below.

1. The Higuchi References Admittedly Show Real-Time Monitoring Before the Filing of the Livak Patents.

Defendants have not cited any art where the term "monitoring" meant only taking readings of a reaction after it is finished. Instead, Defendants argue that one of skill in the art would have understood the word "monitoring" to refer to monitoring during a reaction because "***Defendants have been unable*** to find a single additional reference ***other than the Higuchi references that utilize real time monitoring***" between 1992 and 1996. Motion at 12. Admittedly then, the Higuchi references both show real-time monitoring. Because the Higuchi references were cited in the Livak Patent specifications, one of ordinary skill in the art would have understood that "monitoring" referred to the monitoring during a reaction. *See Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 594 (1993) ("The fact of publication (or lack thereof) in a peer reviewed journal thus will be a relevant, though not dispositive, consideration in assessing the scientific validity of a particular technique or methodology.").

Consequently, based on the Higuchi references, a person of ordinary skill in the art would have understood the term "monitoring the fluorescence" to mean monitoring product generation ***during*** the reaction.

2. Defendants' Belief That an Article is "Not Simple" is Irrelevant.

Defendants assert that one of skill in the art would not have understood that "monitoring"

included monitoring ***during*** reactions because the techniques used in the 1993 Higuchi reference were "not 'simple.'" Motion at 7. Notably, Defendants do not challenge the 1992 Higuchi reference. Moreover, Defendants offer only attorney argument to challenge the peer-reviewed 1993 Higuchi article's own characterization that its test is "simple." Dkt. No. 201-2 at 1026. The standard for claim construction is not whether methods for implementing a construction are simple, but rather, how one of skill in the art would have understood the term.

Defendants also imply that skilled artisans would not have understood "monitoring" as used in the Livak Patents to mean monitoring ***during*** reactions because the Higuchi references did not use dual-labeled probes, but disclosed that they were testing "alternative strategies of detection using optically active probes based on the 5'-3' exonuclease activity of Taq DNA polymerase." *See* Motion at 9-10 (emphasis omitted). While this fact reflects the important role that the Livak Patents played in developing dual-labeled probes for real-time reactions, it says nothing about term "monitoring the fluorescence." Skilled artisans would have been familiar with monitoring fluorescence during reactions and would have known that those words meant.

In sum, the intrinsic and extrinsic evidence shows that skilled artisans not only understood that "monitoring" a PCR reaction meant monitoring during the reaction, but also that artisans were monitoring PCR reactions through a variety of techniques. Defendants' assertion that those of skill in the art would not have understood the meaning of "monitoring" because they do not consider the 1993 Higuchi apparatus "simple" fails.

B. How the Court Interpreted "RT-PCR" is Irrelevant.

Defendants assert that the Court falsely believed that "RT-PCR" meant "real time PCR" instead of "reverse transcriptase PCR" in an article. Motion at 10-11. But what the Court believed the authors meant by "RT-PCR" is irrelevant. The Court's conclusion is that "[t]he mere fact that . . . [a] paper discloses 'a novel 'real time' quantitative PCR method . . . resulting

in much faster and higher throughput assays,' does not mean that there were no other real time quantitative PCR methods already in existence." Order at 17. In fact, that article cites to several pre-1994 articles that used other methods to monitor PCR reactions as they progressed, including the 1992 Higuchi paper. *See* Dkt. No. 192-3 at 994. The Court properly recognized that one of ordinary skill in the art at the time of invention would have understood "monitoring the fluorescence" to have its ordinary meaning. It should affirm its construction.

V. CONCLUSION

Life Tech respectfully requests that the Court affirm Magistrate Judge Everingham's constructions of the three terms at issue.

Dated: October 24, 2011

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned certifies that the foregoing document was filed electronically in compliance with Local Rule CV-5(a). As such, this document was served on all counsel who are deemed to have consented to electronic service. Local Rule CV-5(a)(3)(A). Pursuant to Fed. R. Civ. P. 5(d) and Local Rule CV-5(d) and (e), all other counsel of record not deemed to have consented to electronic service were served with a true and correct copy of the foregoing by email and/or fax, on this the 24th day of October, 2011.

/s/ Cora Louise Schmid